PATENT SPECIFICATION

DRAWINGS ATTACHED

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International Classification:—**B65b. B05. B67b.**

COMPLETE SPECIFICATION

Improvements in or relating to Packages

We, ANCHOR SERUM COMPANY, a corporation organised under the laws of the State of Delaware, United States of America, of Exchange Building, South St. Joseph, Missouri, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to the packaging of biologicals in glass containers.

At the present time biologicals, for example, live virus vaccines, are conventionally packaged in glass bottles under vacuum. The containers are normally closed by an elastomeric stopper which is readily puncturable by the needle of a syringe to effect entry into the bottle. To enhance the sealability of the container and closure a metal ring is usually applied to encompass the area where the bottle top and the closure meet. Despite such precautions, however, it has been found that leaks tend to develop so that oxygen and/or moisture from the air gradually enter the bottle and the potency of the vaccine or other biological adversely affected by air is reduced. This is particularly so in the case of vacuum packages. As a result, the shelf life of such materials is not as long as would be desired and, in fact, many bottles of live virus vaccines, for example, are of weakened potency even before the date stamped thereon which is supposed to indicate the safe period for use of the vaccines.

To overcome these serious problems affecting the shelf life of biologicals various proposals have been made in the past. According to one proposal, a vaccine, for example, is packaged in a glass bottle having two compartments. The vaccine is in one compartment under vacuum and in the other compartment nitrogen is present under pressure so that nitrogen, rather than air, will leak into the portion of the bottle containing the vaccine. This system has not proven too satisfactory since it does not lend itself readily to mass production, the containers are relatively expensive and there is difficulty in adding liquid to the desiccated vaccine since the nitrogen pressure must be overcome.

Another proposal has been to employ a hermetic glass seal between the closure and the bottle. Such a procedure, however, has the disadvantage that the preparation of such a seal is expensive and, furthermore, the doctor or veterinarian runs the risk of cutting himself upon breaking the seal in order to use the vaccine. Despite these disadvantages and the fact that the glass sealed bottles command a premium of several U.S. dollars per bottle, they have been gaining increasing favor among doctors and veterinarians because they do provide considerably longer shelf life for biologicals than do the conventional containers and closures.

The present invention provides a means for sealing glass bottles containing biologicals normally subject to deterioration in air so that the resulting packaged article has increased shelf life.

This invention prevents the leakage of oxygen and/or moisture into glass bottles containing a live virus vaccine under a vacuum.

Further, this invention reduces the risk of breakage of the bottle with attendant release of the contents due to accidental dropping of glass bottles containing biologicals which are adversely affected by air.

This invention also provides a simple and economical procedure for insuring the sealing of glass bottles containing biologicals.

The entire scope of applicability of the present invention will become apparent from the detailed description given hereinafter; it should be understood, however, that the detailed description and specific examples, while indicating preferred embodiments of the in-

vention, are given by way of illustration only, since various changes and modifications within the invention will become apparent to those skilled in the art from this detailed description.

It has now been found that desirable results and advantages can be attained by appropriately sealing stoppered glass containers with a thin film of a normally crystalline vinylidene chloride polymer. Such polymers normally contain over 50% vinylidene chloride and preferably at least 70% vinylidene chloride. The term "polymer" in this specification is used in its normal sense to include homopolymers, copolymers, terpolymers, tetrapolymers and the like. Typical copolymers include vinylidene chloride-acrylonitrile, vinylidene chloride-vinyl chloride (for example, 80 to 20%), vinylidene chloride-ethyl acrylate, vinylidene chloride vinyl chloride-dimethyl maleate, vinylidene chloride-acrylonitrile-isobutylene, vinylidene chloride-butyl methacrylate, etc. The presently preferred vinylidene chloride polymer is "Saran" F-220 ("Saran" is a Registered Trade Mark) (a copolymer containing 80% vinylidene chloride and 20% acrylonitrile and having a viscosity of 60 centipoises as a 20% solution in acetone). "Saran" F-120, both in the 200 centipoises and 1000 centipoises grades, has also been employed successfully. ["Saran" F-120 is a copolymer of vinylidene chloride (80%) and acrylonitrile (20%) having limited solubility in pure acetone but being readily soluble in methyl ethyl ketone or mixtures of methyl ethyl ketone with up to 75% acetone].

The invention will be best understood in connection with the drawings wherein:—

Figure 1 is a side elevation of a glass bottle suitable for coating according to the invention;

Figure 2 is a side elevation of the bottle of Figure 1 after a coating of saran (vinylidene chloride polymer) has been applied to the sealing area;

Figure 3 is a view partially in section of the bottle of Figure 2;

Figure 4 is a side elevation of a bottle treated in a preferred form of the invention; and

Figure 5 is a vertical section of the bottle of Figure 4.

It has been found according to the invention that the leakage of air or moisture into a glass bottle containing a biological can be prevented if the seal area is coated with a thin layer of a normally crystalline vinylidene chloride polymer. This result is obtained even in the case of vacuum packages. In the art, such packages normally have a vacuum of 1 mm. or less and usually below 50 microns and down to 1 micron.

The glass bottle can have a glass stopper, but it has been found preferable to employ elastomeric or plastic stoppers which are adapted to permit the entry of the needle portion of a syringe into the glass bottle. It has been found that there is leakage of oxygen into such vacuum packages through the penetrable stopper and, hence, to ensure the utmost in shelf life or stability of the biological, it has been found preferable to coat the entire stopper and not merely the sealing area.

If the entire glass bottle and stopper are coated with the normally crystalline vinylidene chloride polymer, it has been unexpectedly found that in the event the bottle is accidently dropped, it will not shatter and permit the escape of the contents but instead the thin film of the normally crystalline vinylidene chloride polymer prevents such shattering of the bottle and scattering of the contents and holds the cracked glass together.

The film of normally crystalline vinylidene chloride polymer can be extremely thin. Preferably, it is at least 0.0025 millimetre thick. Thicker films can be employed but generally there is not a sufficient improvement in properties to warrant the expenses of using films more than 0.025 or 0.05 millimetre in thickness.

The normally crystalline vinylidene chloride polymer can be applied to the surface of the glass container and closure by dipping the closed container in an organic solution or aqueous dispersion of the polymer or the polymer can be sprayed onto the container and closure from such solution or dispersion. The use of an aqueous dispersion of the polymer, for example, vinylidene chloride acrylonitrile copolymer, has the advantage that the drying step does not involve the removal of toxic or inflammable vapors.

"Saran" F-220 is advantageous applied as a 20% solution in acetone. Since acetone is extremely volatile, it is readily removed.

"Saran" F-120 (200 centipoises) is advantageous applied as a mixture of 15 parts of the resin dissolved in a mixture of 65 parts acetone and 20 parts methyl ethyl ketone.

Measles vaccine and canine distemper vaccine are notoriously unstable despite all precautions taken in packaging. However, when a "Saran" coating was applied according to the present invention to stoppered glass bottles containing such vaccines there was a considerable improvement in their stability.

As typical biologicals which can be packaged according to the invention, there may be mentioned vaccines such as modified live hog cholera vaccine, modified live canine distemper vaccine, live canine infectious hepatitis vaccine, live brucella abortus vaccine, infectious bovine rhinotracheitis virus vaccine, killed canine distemper vaccine, typhoid-paratyphoid vaccine, rabies vaccine, Newcastle vaccine (live), bronchitis vaccine (for chickens), influenza vaccine, diphtheria toxoid combined

with pertussis, undulant fever vaccine, Rocky Mountain Spotted Fever vaccine, typhus vaccine, equine encephalomyelitis vaccine, smallpox vaccine, anthrax vaccine, blackleg vaccine, erysipelothrix rhusiopathiae vaccine, clostridium chauvei-septicus vaccine, oral measles vaccine, oral poliomyelitis vaccine, etc. Other biologicals, such as gamma globulin, and blood serum, hormones, for example, folic acid, unstable vitamins and the like, can likewise be packed in this manner.

The term "vaccine" is employed as defined in Kirk-Othmer "Encyclopedia of Chemical Technology", Volume 14, pages 488—503, and the term "biologicals" is employed as defined in Volume 10, pages 245—247, of Kirk-Othmer.

The biologicals are usually freeze dried and then vacuum packaged prior to applying the external saran coating to the glass bottle and stopper.

Referring more specifically to Figures 1—3 of the drawings, there is provided a cylindrical glass bottle 2 having a neck 4 of reduced diameter and terminating at its upper end in an external beaded portion 6 surrounding central opening 7. A biological for example, live canine distemper virus vaccine, is placed in the bottle and freeze dried. Then a vacuum, for example, of 25 microns, is applied and closure 8 is applied to plug the opening while the bottle is under vacuum. Closure 8 comprises a conventional rubber stopper 10 having a metal, for example, aluminium, covering 12 therefor. The stopper 10 has a downward depending flange 13 which closely fits the inner wall of the upper portion of the neck 4. The metal covering 10 has a skirt 14 which closely fits the external beaded wall 6 of the upper portion of the neck 4. The bottle is spun upon application of the closure and the terminal portion of the skirt 14 is locked under the bead 6 in conventional manner. The central portion 16 of the stopper 10 is relatively thin and is not covered by the aluminium cover so that it is possible for a syringe needle to be readily inserted therethrough. This is a standard commercial vaccine bottle.

After the closure is applied to the bottle as described, "Saran" F-220 as a 20% solution in acetone is sprayed on the upper portion of the container to form a coating 18 of the "Saran" F-220. It is essential that this "Saran" coating cover the area 20 where the skirt 14 joins the glass bottle. This area is defined herein as the seal area. The "Saran" F-220 solution should also be sprayed over the top of the closure also in order to prevent leakage through the stopper 10. As shown in Figures 2 and 3, the "Saran" F-220 is actually applied to the entire neck portion of the bottle and the entire top of the closure so that the closure is completely encased thereby. The volatile solvent is readily removed leaving the impervious "Saran" film coating having a thickness of 0.005 millimetre adhering to the glass bottle and the closure.

Figures 4 and 5 show a preferred form of the invention wherein the impervious "Saran" coating 22 encases the entire bottle 2 and stopper 10. As shown in Figures 4 and 5, the metal cover 12 can be omitted. The bottle in Figure 5 has spray dried attenuated hog cholera virus vaccine (rabbit origin) 24 therein under a vacuum of 20 microns. The "Saran" coating 22 is made of "Saran" F-120 (200 centipoises) and is applied by dipping the stoppered glass bottle in a bath containing 15 parts "Saran" F-120, 65 parts acetone and 20 parts methyl ethyl ketone. The solvent is then permitted to evaporate to leave the impervious "Saran" F-120 coating, for example, of 0.025 millimetre. As previously explained, in the event the bottle 2 and closure 10 encased in saran film 22 should be dropped, the glass would not shatter but would be held together by the saran coating.

The thin "Saran" coating, however, offers little resistance to the needle of the syringe when it is desired to utilize the contents of the bottle.

WHAT WE CLAIM IS:—

1. A package having long shelf life comprising a glass container having an opening therein, a closure therefor, a biological as hereinbefore defined subject to attack by the atmosphere in said container, and a coating of a normally crystalline vinylidene chloride polymer at least around the juncture of the terminal external portion of said closure and said container to prevent access of the atmosphere to the contents of said container.

2. A package according to Claim 1 wherein the coating of a normally crystalline vinylidene chloride polymer encases said closure and adheres to said container to prevent access of the atmosphere to the contents of the container.

3. A package according to Claim 1 wherein the closure comprises material permitting ready entry of a syringe needle therethrough.

4. A package according to Claim 3 wherein said closure is selected from elastomers and plastics which are adapted to permit ready entry of a syringe needle therethrough and wherein there is a vacuum of less than 1 mm. in said container.

5. A package according to Claim 1 or 2 having enhanced resistance to breakage wherein the film of normally crystalline vinylidene chloride polymer completely encases said container and said closure to prevent access of the atmosphere to the contents of said container.

6. A package according to any one of Claims 1, 2 or 3 wherein there is a vacuum in said container.

7. A package according to Claim 6 wherein said biological is a vaccine and the vacuum is less than 1 mm.

8. A package as herein described and shown in Figs. 1 to 3 of the annexed drawing.

9. A package as herein described and shown in Figs. 4 and 5 of the annexed drawing.

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890984 COMPLETE SPECIFICATION
1 SHEET *This drawing is a reproduction of the Original on a reduced scale*

FIG.1.

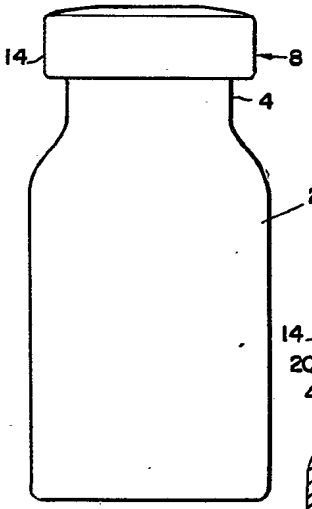

FIG.2.

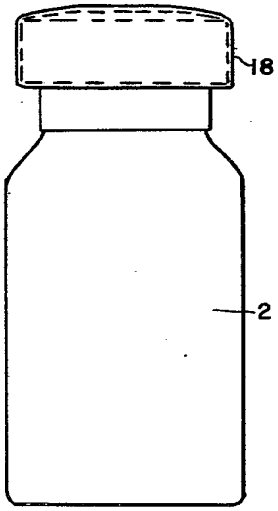

FIG.3.

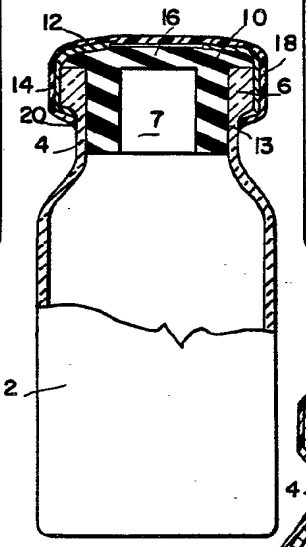

FIG.4.

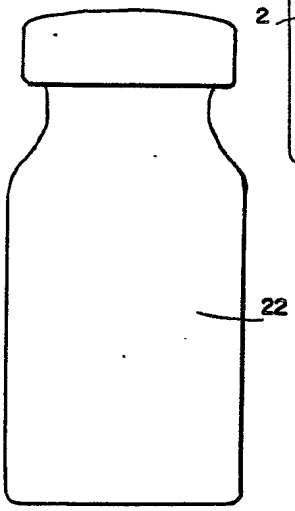

FIG.5.